REMARKS

Applicants herein amend the application to clarify and more accurately recite the nomenclature of the ribonucleases disclosed in the specification. In the specification, Applicants recite bovine ribonuclease A and human ribonuclease A. However, it is known in the art that the human homolog of bovine ribonuclease A is known as ribonuclease I (See Raines, R.T., Ribonuclease A 98:1045-1065 (1998)). Accordingly, Applicants have amended the specification and claims to recite, where appropriate, that "ribonuclease I" when referring to the human homolog of bovine ribonuclease A. Applicants have also amended claims 8, 11, 22, 25, 38, and 41, to recite "ribonuclease I" in accordance with the nomenclature used in this art. Accordingly, Applicants submit that no new matter is added herewith. Marked-up copies of the amended paragraphs are shown in Appendix I attached hereto.

Following entry of the present amendment, claims 1-3, 5-11, 13-17, 19-25, 27-33, 35-41, and 43-45 remain in the application for consideration. Claims 4, 12, 18, 26, 34, and 42 are herein cancelled without prejudice or disclaimer. Original claims 46-57 were cancelled without prejudice in the Reply submitted by Applicants on April 26, 2002. Claims 1, 8, 9, 10, 11, 14, 15, 22, 23, 24, 25, 28, 30, 31, 33, 38, 39, 40, and 41 are herein

amended. Marked-up versions of the amended claims are shown in Appendix II. No new matter is added herewith.

In response to the Restriction/Election Requirement (Paper #6), Applicants chose to prosecute the claims of Group I (claims 1-45), and elected the species of copolymer, nucleic acids, wild type S-protein fragment of bovine or human ribonuclease A, growth factors, and water. Applicants submit that elections made in response to the Restriction/Election requirement (Paper 6), apply to all claims on which the elected species are readable. However, the Examiner indicated that claims 10, 24, and 40 were withdrawn from Examination as being directed to a nonelected species.

Applicants respectfully point out that "growth factors" was selected as the species election with respect to the targeting portion of the invention recited in claim 9. Further, Applicants submit that claims 10, 24, and 40, all directed to vascular endothelial growth factor 121, are readable on the selected species of "growth factors" recited in claims 9, 23, and 39, respectively. Therefore, Applicants respectfully request that claims 10, 24, and 40 be reinstated and examined in the instant application. To expedite the prosecution of this application, Applicants direct their Reply to all the claims pending in the application (claims 1-45).

Rejections under 35 USC §112

Claims 4, 18, and 34 were rejected as lacking enablement. Applicants herein cancel claims 4, 18, and 34 without prejudice, and now submit that this rejection is moot.

Claims 1-9, 11-23, 25-39, and 41-45 were rejected because it was alleged that the specification, while being enabling for compositions and methods for delivering diagnostic and research compounds to a target, did not provide enablement for compositions and methods for delivery of therapeutic compounds. Applicants submit that this rejection is improper and goes beyond the scope of the claims. Therefore, Applicants submit that this rejection is untenable and should be withdrawn.

Applicants submit that the present invention is directed to a molecular delivery vehicle for delivery of therapeutic, diagnostic, or research compounds to a target, comprising: (a) a carrier for carrying the compounds; (b) an adapter covalently linked to the carrier; and (c) a targeting protein comprising a recognition portion and a targeting portion, the recognition portion comprising an S-peptide fragment of bovine or human ribonuclease A and being capable of binding to the adapter, the targeting portion capable of binding to the target (emphasis supplied). The present invention is also directed to

pharmaceutical compositions comprising the above molecular delivery vehicle; an article of manufacture comprising packaging material and a pharmaceutical agent containing the above molecular delivery vehicle; and a method for delivering therapeutic, diagnostic, or research compounds to a target, comprising the steps of administering a pharmaceutical composition comprising, among other things, the above molecular delivery vehicle.

Applicants submit that this rejection appears to be based on the apparent lack of successful implementation of "gene therapy protocols" in the art at the time the invention was made. Applicants submit that the present invention is not directed to a gene therapy protocol, or any method of treating diseases using therapeutic DNA molecules. Rather, the present invention is directed to a molecular delivery vehicle that is designed to deliver compounds to a target and methods of delivering those compounds to targets. In other words, Applicants are not claiming gene therapy protocols, treatments of diseases, or expression of therapeutic DNAs, but rather compositions and methods useful for delivering compounds to targets.

Applicants submit that the scope of the presently claimed invention is fully enabled by virtue of the numerous examples

describing, among other things, preparation of fusion proteins comprising S-peptide or S-protein linked to VEGF, preparation of liposomes carrying S-protein fragment of ribonuclease, preparation of conjugates of polyethyleneimine with S-protein fragment of ribonuclease, functional activity of complexes of lip(DOX)-SP with FVEGF121, preparation of complexes of DNA with PEI-SP conjugates and FVEGF121, liposome delivery by DNA/PEI-SP-FVEGF121 complexes, and DNA delivery by DNA/PEI-SP-FVEGF121 complexes. In particular, Examples 6 and 7 clearly describe delivery of a drug-loaded liposome and DNA complexed with PEI to cells, and such examples, in combination with the entire written description of the present invention, enables the claimed scope of the present invention.

Therefore, Applicants contend that the present rejection and the conclusion

> "one of skill in the art could not use the claimed methods and compositions commensurate in scope with the claims"

goes beyond the scope of the claims of the present invention, and should be withdrawn.

Claims 12, 26, 31-39, and 41-45 were rejected as being indefinite for various reasons. With respect to claims 12, 26, and 42, Applicants herein cancel these claims without prejudice,

and now submit that this rejection is moot. With respect to claims 31-39 and 41-45 and the issue of methods steps, Applicants herein amend claim 31 to recite administering a pharmaceutical composition to a patient, and a step directed to delivery of compounds to a target. Applicants submit that this rejection is now overcome. With respect to claim 33, Applicants herein amend this claim to correct the typographical errors, and now submit that this rejection is overcome.

Rejections under 35 USC §102

Claims 1-3, 5-9, 13-17, 19-23, 27-29, 31-33, 35-39, and 43-45 were rejected as being anticipated by U.S. Patent No. 4,885,172 to Bally et al. Applicants respectfully traverse the rejection.

Bally et al. disclose a composition for targeting, storing and loading of liposomes consisting of liposomes covalently or non-covalently coupled to the glycoprotein streptavidin. The streptavidin is coupled to biotinylated proteins made by chemical modifications. Examples of such chemically modified proteins include biotinylated immunoglobulin G or biotinylated monoclonal antibodies. In the rejection, it was asserted that the liposome acts as the carrier, the adapter is streptavidin, and the targeting protein is an antibody, having a recognition

portion (e.g., the biotin) and a targeting portion (e.g., the rest of the antibody).

Applicants herein amend claims 1, 15, 30, and 31 to more concisely describe the targeting protein component of the invention. No new matter is added herewith. In particular, claims 1, 15, 30, and 31, as well as claims depending therefrom, are herein amended to recite a recombinant targeting fusion protein and that is made from a recognition portion, that consists essentially of a recognition peptide, and a targeting portion that is capable of binding to the target.

Applicants submit that Bally et al. does not disclose or suggest the present invention as now claimed. In particular, Bally et al. does not disclose or suggest a recombinant targeting fusion protein as disclosed and claimed by Applicants, but rather a chemically modified protein. Applicants submit that the phrase "fusion protein" is defined in the specification at page 13, lines 4-7, wherein it is stated:

> a fusion protein refers to a recombinant protein that contains two or more polypeptide fragments that are encoded by DNA sequences that have been combined with the methods of recombinant DNA technology in a form that allows expression of the fusion protein in suitable hosts. (Emphasis supplied)

Thus it is clear that the recombinant fusion protein recited in the claims of the present invention is

distinguishable from the chemically modified (e.g., biotinylated) antibodies disclosed by Bally et al.

Further, Applicants have amended the claims to recite that the recognition portion of the targeting fusion protein consists essentially of a recognition peptide to further clarify the nature of the recognition portion, and to further distinguish the reference of Bally et al. which discloses a chemical moiety as a "recognition portion". Applicants submit that the term "recognition peptide" as used in the presently claimed invention, is explicitly defined in the specification at page 13, lines 1-3, wherein it is stated that a recognition peptide can be introduced into a fusion protein using the methods of recombinant DNA technology. Moreover, the term "peptide" is generally known in the art to consist of up to 100 amino acid residues. For example, the U.S. Patent and Trademark Office defines a peptide as a compound containing a sequence of 4-100 amino acid units which are bound through at least one normal peptide link (See USPTO Patent Classification, Class 930, available at http://www.uspto.gov/go/classification/uspc930/defs930.htm). Accordingly, Applicants submit that the presently claimed invention is distinguishable from Bally et al., and therefore this rejection is overcome.

Claims 1-3, 5-7, 9, 12-17, 19-21, 23, 26-29, 31-33, 35-37, 39, 42, 44 and 45 were rejected as being anticipated by Tillman et al. (J. Immunol. Vol. 162, pp 6378-6383 (1999)). Applicants respectfully traverse the rejection.

Tillman et al. disclose methods and compositions for gene transfer, wherein adenoviruses carry diagnostic nucleic acids encoding luciferase. Tillman et al. further disclose that a bispecific antibody which recognizes the adenovirus fiber protein knob domain and the cell surface target CD40 is used as a targeting protein. Significantly, at page 6379, lines 19-25, it is stated that the bispecific antibodies are made by chemical crosslinking with SPDP.

In the rejection, it was asserted that the knob domain is considered the adapter, the fiber protein and adenovirus is considered the carrier, and the bispecific antibody is considered the targeting protein, wherein the portion of the bispecific antibody that recognizes the knob domain is considered to be the recognition portion, and the portion of the bispecific antibody that recognizes CD40 is considered to be the targeting portion.

As indicated above, Applicants herein amend claims 1, 15, 30, and 31 to recited that the targeting protein of the invention is a recombinant targeting fusion protein made from a

recognition portion consisting essentially of a recognition peptide, and a targeting portion capable of binding to said target.

Applicants submit that Tillman et al. is distinguishable from the presently claimed invention. In the present invention, the targeting protein is a recombinant fusion protein. Tillman, by contrast, utilizes chemical crosslinking of two independent antibodies to construct the bispecific antibody, which produces a different product than the recombinant targeting fusion protein recited in the claims of the present invention. Moreover, Tillman et al. does not disclose or suggest use of a genetically fused peptide as the recognition portion. Rather, Tillman et al. use a bulky antibody. Accordingly, Applicants submit that the claims, as amended, are not anticipated by Tillman et al., and that this rejection is overcome.

Claims 1-3, 6, 7, 9, 12, 14-17, 19-21, 23, 26, 28, 29, 31-33, 35-37, 39, 42, 44, and 45 were rejected as being anticipated by U.S. Patent No. 5,712,136 to Wickham et al. Applicants respectfully traverse the rejection.

Wickham et al. discloses methods for adenoviral-mediated cell targeting using the adenovirus base protein. In the disclosure at Col. 9, lines 6-16, Wickham et al. disclose use of a "bispecific molecule" which is composed of a first component

that binds a binding domain of a pentose base protein, and a second component that binds to a cell surface binding site. At Col. 9, lines 20-24, Wickham et al. further disclose that the first and second components of the bispecific molecule are covalently linked to each other (e.g., a covalent linkage such as a chemical linkage or fusion). Further, in Example 12 at Col. 32, lines 18-60, and the description of Figure 4 at Col. 5, lines 23-33, it is disclosed that a bispecific antibody was constructed by chemically linking the M2 mAb with L230 mAb.

At Col. 3, line 59, and continuing to Col. 4, line 3, Wickham et al. also disclose a composition comprising an adenovirus having a modified fiber protein and a bispecific antibody which recognizes a modified fiber protein and a target antigen. According to the rejection, the portion of the fiber protein to which the antibody binds is considered the adapter, which is covalently bound to the adenovirus carrier. The bispecific antibody is considered to be a targeting protein having a recognition portion (being the portion of the antibody that recognizes the fiber protein) and a targeting portion (being the portion of the antibody that recognizes the target).

Applicants submit that, like Tillman, the Wickham et al. is distinguishable from the presently claimed invention. In the present invention, the targeting protein is a recombinant fusion

protein having a recognition portion consisting essentially of a peptide. By contrast, Wickham et al. utilizes chemical crosslinking of two independent antibodies to construct the bispecific antibody. This process results in a clearly different product than the recombinant targeting fusion protein recited in the claims of the present invention. Moreover, Wickham et al. does not disclose or suggest use of a genetically fused peptide as the recognition portion. Accordingly, Applicants submit that the claims, as amended, are not anticipated by Wickham et al., and that this rejection is overcome.

Rejections under 35 USC §103

Claim 30 was rejected as being unpatentable over either one of U.S. Patent No. 4,885,172 to Bally; Tillman et al. (J. Immunol. Vol. 162, pp 6378-6383 (1999)); or U.S. Patent No. 5,712,136 to Wickham et al. Applicants respectfully traverse the rejection.

Claim 30, as amended, recites an article of manufacture comprising packaging material and a pharmaceutical agent contained within said packaging material, wherein said pharmaceutical agent is therapeutically effective for treating pathophysiological conditions that depend on cells that can be

detected or affected via target-mediated delivery of therapeutic or diagnostic compounds and wherein said packaging material comprises a label which indicates that the pharmaceutical agent can be used for treating pathophysiological conditions that depend on cells that can be detected or affected via target-mediated delivery of therapeutic or diagnostic compounds, and wherein said pharmaceutical agent comprises a pharmaceutically effective amount of a molecular delivery vehicle for delivery of therapeutic, diagnostic, or research compounds to a target, comprising:

(a) a carrier for carrying said compounds;
(b) an adapter covalently linked to said carrier; and
(c) a recombinant targeting fusion protein comprising a recognition portion and a targeting portion, said recognition portion consisting essentially of a recognition peptide, and capable of binding to said adapter, said targeting portion capable of binding to said target;

in a pharmaceutically acceptable carrier.

Applicants submit that none of the cited references, taken individually or in any combination, disclose or suggest the invention as now claimed. In particular, none of the references disclose or suggest a recombinant targeting fusion protein comprising a recognition portion and a targeting portion,

wherein the recognition portion consists essentially of a recognition peptide, and capable of binding to said adapter, the targeting portion capable of binding to the target. Accordingly, Applicants submit that claim 30, as amended, is not obvious in view of Bally et al., Tillman et al., or Wickham et al., taken individually or in any combination. Accordingly, Applicants submit that this rejection is overcome.

In view of the above amendments and remarks, Applicants submit that the claims are in condition for allowance, and respectfully request reconsideration and early receipt of a Notice of Allowance.

SPECIFICATION AMENDMENTS UNDER 37 CFR §1.121(b)(iii)

Please REWRITE the paragraph at page 5, lines 12-19, as follows:

In another aspect, the present invention is directed to an isolated nucleic acid sequence, comprising (i) a first nucleic acid sequence segment encoding 1 to 15 amino acid residue N-terminal peptide fragment (S-peptide) of bovine or human ribonuclease A <u>(the human homolog of bovine ribonuclease A is also known as ribonuclease I as described in Raines, R.T., Ribonuclease A 98:1045-1065 (1998))</u>, and (ii) a second nucleic acid sequence segment encoding any full-length or mutated isoform of human vascular endothelial growth factor (VEGF), wherein the isolated nucleic acid sequence codes for a fusion protein which specifically binds adapter protein recognized by the polypeptide encoded by the first nucleic acid, and specifically binds to receptors for vascular endothelial growth factor recognized by the polypeptide encoded by the second nucleic acid sequence.

Please REWRITE the paragraph at page 13, lines 8-23, as follows:

As used herein interchangeably, "S-peptide fragment of ribonuclease", "S-peptide", or "S-tag" refers to a 15 amino acid fragment of bovine pancreatic ribonuclease A with the following

amino acid sequence: Lys-Glu-Thr-Ala-Ala-Ala-Lys-Phe-Glu-Arg-Gln-His-Met-Asp-Ser (SEQ ID NO:1), or to a 15 amino acid fragment of human ribonuclease A (also known as ribonuclease I as indicated above) with the following amino acid sequence: Lys-Glu-Ser-Arg-Ala-Lys-Lys-Phe-Gln-Arg-Gln-His-Met-Asp-Ser (SEQ ID NO:2), that can associate with the S-protein fragment of ribonuclease A forming the associate known as ribonuclease S for bovine protein. It is understood that the S-peptide may be used as modified by amino acid substitutions, amino acid deletions, amino acid insertions, and amino acid additions, as in fusion protein that do not eliminate the ability of the peptide to bind to S-protein fragment of ribonuclease. Such operational definition of S-peptide encompasses peptide fragments from ribonucleases of other species that may bind to appropriate protein fragment. Vectors for the expression of fusion proteins with bovine S-tag are commercially available. Vectors for the expression of fusion proteins with human S-tag are constructed using techniques known in the art by insertion of DNA sequence encoding the human S-tag with the composition Lys-Glu-Ser-Arg-Ala-Lys-Lys-Phe-Gln-Arg-Gln-His-Met-Asp-Ser (SEQ ID NO:2) in the commercially available expression vectors.

Please REWRITE the paragraph at page 29, lines 7-9, as follows:

The primers corresponding to the "sense" strand of human ribonuclease A cDNA (SEQ ID NOS:14, 15, and 16) included AUG codon immediately upstream of the DNA codon for amino acid 16,

19, and 21 of the human ribonuclease A (also known as ribonuclease I), respectively.

Please REWRITE the paragraph at page 32, lines 13-23, as follows:

A single-stranded DNA fragment (SEQ ID NO:27) corresponding to the "sense" strand of human ribonuclease A (also known as ribonuclease I) cDNA encoding S-peptide Lys-Glu-Ser-Arg-Ala-Lys-Lys-Phe-Gln-Arg-Gln-His-Met-Asp-Ser (SEQ ID NO:28) and a complementary single-strand DNA fragment (SEQ ID NO:29) were mixed at equimolar concentrations and annealed at room temperature for 10 min. The fragments were designed to reconstitute 5'- Nde I site upstream of K1 codon and 3'-Kpn I site downstream of S15 codon after annealing. The annealed DNA fragment was ligated into a pET/VEGF121 vector between Nde I and the Kpn I sites. The resulted plasmid was designated pET/hus-VEGF121, and transformed into NovaBlue competent cells (Novagen, USA) according to the manufacturer's instructions. Bacterial cultures containing the desired plasmids were grown further in order to obtain large preparations of isolated plasmids using methods described in Example 1.A.2.

Please REWRITE the paragraph beginning at page 33, line 27 and continuing to page 34, line 20, as follows:

To purify each of VEGF fusion proteins a corresponding cell culture pellet obtained as described in Example 1.C.1 was resuspended in ice cold buffer A (50 mM Tris-HCl pH 7,5, 0.1 mM $MgCl_2$, 0.1 mM DTT, 200 mg/L PMSF, 25 mg/L antitripsin, 50 mg/L leupeptin, 25 mg/L aprotinin). After five cycles of freezing and thawing DNAse was added to the cell suspension, 50 U per ml. The suspension was incubated for 20 min at room temperature; then centrifuged at 5,000xg for 30 min at 4°C. The inclusion bodies pellet was solubilized in 10 ml of 8 M urea, followed by sonication for 5-10 min in an ice-cold water sonicator (FC 14, Fisher Sci., USA) and the protein solution was clarified by centrifugation at 14,000xg for 10 min, at 4°C, and the supernatant was dialyzed against 10 mM Tris-HCl pH 8.0, 150 mM NaCl for 16 hours at 4°C. VEGF fusion proteins obtained as described here were 75-90% pure as judged by Coumassie-stained SDS-PAGE analysis. VEGF fusion proteins containing thioredoxin were designated txVEGF121, txVEGF165, and txVEGF189. VEGF fusion proteins without thioredoxin were designated FVEGF121, FVEGF165 and FVEGF189. The fusion protein consisting of 16-124 aa fragment of bovine ribonuclease A linked to human VEGF121 via 7 aa linker GTDDDDK (SEQ ID NO:30) was designated 16-BoS-VEGF121. The fusion protein consisting of 1-15 aa fragment of human ribonuclease A (also known as ribonuclease I) linked to human VEGF121 via 7 aa linker GTDDDDK was designated hus-VEGF. The concentrations of VEGF fusion protein with bovine S-tag were measured with a commercially available S-tag Rapid Assay Kit (Novagen, USA) based on quantitation of ribonuclease activity which is restored when a protein carrying the S-peptide fragment of ribonuclease (S-tag) is supplemented with the S-protein fragment of ribonuclease. Concentration of hus-VEGF was

determined by SDS-PAGE with FVEGF121 as a standard. Solutions of all VEGF fusion proteins were supplemented with glycerol to a final concentration of 10% v/v and stored in aliquots at -20°C. Schematic representations of the VEGF fusion proteins comprising the S-peptide or S-protein fragment of ribonuclease linked to the N-terminus of the corresponding vascular endothelial growth factor via a peptide spacer are presented in FIG. 2.

Please REWRITE the paragraph at page 36, lines 1-3, as follows:

5. Expression and Purification of Recombinant Protein HuS/C Containing a Mutant 18-125 Amino Acid Fragment of Human Ribonuclease A (Ribonuclease I) with S(19,20)A and S123C Amino Acid Substitutions.

APPENDIX II

CLAIM AMENDMENTS UNDER 37 CFR §1.121(c)

Please REWRITE claims 1, 8, 9, 10, 11, 14, 15, 22, 23, 24, 25, 28, 30, 31, 33, 38, 39, 40, and 41 as follows:

1. (Amended) A molecular delivery vehicle for delivery of therapeutic, diagnostic, or research compounds to a target, comprising:
   (a) a carrier for carrying said compounds;
   (b) an adapter covalently linked to said carrier; and
   (c) a recombinant targeting fusion protein comprising a recognition portion and a targeting portion, said recognition portion consisting essentially of a recognition peptide, and capable of binding to said adapter, said targeting portion capable of binding to said target.

8. (Amended) The molecular delivery vehicle of claim 1, wherein said adapter is selected from the group consisting of a wild type or mutant S-protein fragment of bovine [or human] ribonuclease A or ribonuclease I, cellulose, calmodulin, and streptavidin.

9. (Amended) The molecular delivery vehicle of claim 1, wherein said targeting portion of said recombinant targeting fusion protein is selected from the group consisting of cytokines, growth factors, peptide hormones, antibodies, fusion proteins, and combinations thereof.

10. (Amended) The molecular delivery vehicle of claim 1, wherein said targeting portion of said recombinant targeting fusion protein is vascular endothelial growth factor 121.

11. (Amended) The molecular delivery vehicle of claim 1, wherein said recognition portion of said recombinant targeting fusion protein is an S-peptide fragment of bovine [or human] ribonuclease A or ribonuclease I.

14. (Amended) The molecular delivery vehicle of claim 1, wherein said recombinant targeting fusion protein further comprises a spacer peptide positioned between said recognition portion and said targeting portion.

15. (Amended) A pharmaceutical composition, comprising:
(1) a pharmaceutically acceptable carrier; and
(2) a pharmaceutically effective amount of a molecular delivery vehicle for delivery of therapeutic, diagnostic, or research compounds to a target, comprising:
(a) a carrier for carrying said compounds;
(b) an adapter covalently linked to said carrier; and
(c) a recombinant targeting fusion protein comprising a recognition portion and a targeting portion, said recognition portion consisting essentially of a recognition peptide, and capable of binding to said adapter, said targeting portion capable of binding to said target.

22. (Amended) The pharmaceutical composition of claim 15, wherein said adapter is selected from the group consisting of a wild-type or mutant S-protein fragment of bovine [or human] ribonuclease A or ribonuclease I, cellulose, calmodulin, and streptavidin.

23. (Amended) The pharmaceutical composition of claim 15, wherein said targeting portion of said recombinant targeting fusion protein is selected from the group consisting of cytokines, growth factors, peptide hormones, antibodies, f usion proteins, and combinations thereof.

24. (Amended) The pharmaceutical composition of claim [18] 15, wherein said targeting portion of said recombinant targeting fusion protein is vascular endothelial growth factor 121.

25. (Amended) The pharmaceutical composition of claim 15, wherein said recognition portion of said recombinant targeting fusion protein is an S-peptide fragment of bovine [or human] ribonuclease A or ribonuclease I.

28. (Amended) The pharmaceutical composition of claim 15, wherein said recombinant targeting fusion protein further comprises a spacer peptide positioned between said recognition portion and said targeting portion.

30. (Amended) An article of manufacture comprising packaging material and a pharmaceutical agent contained within said

packaging material, wherein said pharmaceutical agent is therapeutically effective for treating pathophysiological conditions that depend on cells that can be detected or affected via target-mediated delivery of therapeutic or diagnostic compounds and wherein said packaging material comprises a label which indicates that the pharmaceutical agent can be used for treating pathophysiological conditions that depend on cells that can be detected or affected via target-mediated delivery of therapeutic or diagnostic compounds, and wherein said pharmaceutical agent comprises a pharmaceutically effective amount of a molecular delivery vehicle for delivery of therapeutic, diagnostic, or research compounds to a target, comprising:

(a) a carrier for carrying said compounds;

(b) an adapter covalently linked to said carrier; and

(c) a recombinant targeting fusion protein comprising a recognition portion and a targeting portion, said recognition portion consisting essentially of a recognition peptide, and capable of binding to said adapter, said targeting portion capable of binding to said target;

in a pharmaceutically acceptable carrier.

31. (Amended) A method for delivering therapeutic, diagnostic, or research compounds to a target in a patient, comprising the [step] steps of:

administering a pharmaceutical composition to said patient, said pharmaceutical composition comprising:

(1) a pharmaceutically acceptable carrier; and

(2) a pharmaceutically effective amount of a molecular delivery vehicle for delivery of compounds to a target, comprising:

(a) a carrier for carrying said compounds;

(b) an adapter covalently linked to said carrier; and

(c) a recombinant targeting fusion protein comprising a recognition portion and a targeting portion, said recognition portion consisting essentially of a recognition peptide, and capable of binding to said adapter, said targeting portion capable of binding to said target; and

permitting said molecular delivery vehicle to contact said target to deliver said compounds to said target in said patient.

33. (Amended) The method of claim 31, wherein said target is [a target is] a cell surface receptor or a cell surface antigen.

38. (Amended) The method of claim 31, wherein said adapter is selected from the group consisting of wild-type or mutant S-protein fragment of bovine [or human] ribonuclease A or ribonuclease I, cellulose, calmodulin, and streptavidin.

39. (Amended) The method of claim 31, wherein said targeting portion of said recombinant targeting fusion protein is selected from the group consisting of cytokines, growth factors, peptide hormones, antibodies, fusion proteins, and combinations thereof.

40. (Amended) The method of claim 31, wherein said targeting portion of said recombinant targeting fusion protein is vascular endothelial growth factor 121.

41. (Amended) The method of claim 31, wherein said recognition portion of said recombinant targeting fusion protein is an S-peptide fragment of bovine [or human] ribonuclease A or ribonuclease I.

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